Vitamin D for each 1.2 g of calcium salt, calculated as elemental calcium.--

REMARKS

Claims 1-8 and 13-18 were rejected under 35 U.S.C. 103(a) as being unpatentable over Meignant et al. (Meignant) in view of Andoh et al.(Andoh) or Tovey or Remington.

Reconsideration is requested.

The Examiner applied Meignant as describing the combination of calcium and Vitamin D within the range claimed by the applicants. The amount of calcium/Vitamin D disclosed by Meignant is not within the applicants' claims because the applicants' claims require a minimum amount of 500 I.U. of Vitamin D with a minimum amount of 1g of calcium. In addition, the claims point out that a ratio of 1-2g of calcium to 500 to 1000 I.U. of Vitamin D is present.

Meignant describes the use of 4mg or 400 I.U. of Vitamin D and 0.5g of calcium and does not disclose any composition having more than 400 I.U. of Vitamin D. Thus, the ratio of 0.5g of calcium/400 I.U. of Vitamin D is described by Meignant. However, the present claims point out a minimum amount of 500 I.U. of Vitamin D. For this reason, the ratio of 0.5g of calcium/400 cannot fall within a claim which requires a minimum of 1g of calcium and a minimum of 500 I.U. of Vitamin D. If 2g of calcium is used according to the applicant's claims, it must be used with 500 to 1000 I.U. of Vitamin D. If the ratio of 2g/1000 I.U. of Vitamin D is reduced to 1g/500 I.U. of Vitamin D, the maximum value of 0.5g/400 I.U. of Vitamin D as disclosed by Meignant is substantially below the value of claim 1.

Meignant refers to a pharmaceutical composition which must be prepared in a "humid environment" (see claim 4, page 11). Further, it is well known in the art that the use of a humid process of preparation can leave traces of humidity in the granules, which may result in a degradation of the

Vitamin D, which undergoes spontaneous oxidation. Claim 1 has been amended to exclude the possible presence of water in the product which further distinguishes the subject matter of claim 1 from Meignant.

The preferred calcium salt is calcium phosphate and its analogs, i.e. compounds that have a high content of calcium but are insoluble. The calcium salts used in the prior art were granulated to avoid poor flow characteristics. This made them unsuitable for processing using ordinary high output machines. However, when used in suspensions, these granules increased the rate of sedimentation causing a "sand effect", thereby decreasing the uniformity of the distribution of the active ingredients within the product. In order to make pharmaceutical compositions for oral use that do not present a "sand effect" it is necessary to identify the exact additives that show acceptable texture, and at the same time allow for an industrial preparation of the composition. Therefore, it was necessary to utilize binders that would be effective in a dry environment, with high concentrations of an insoluble calcium salt such as calcium phosphates. These conditions and binders are not disclosed in Meignant.

The Andoh patent describes the use of a granulation technique in making tablets. Various binders are described but there is no mention of the problems that arise when polyvinylpyrrolidone (PVP) is used in the preparation of a Vitamin D/calcium phosphate granulation. The polyethylene glycol that is mentioned by Andoh as "equivalent" to PVP is PEG 6000 which is quite different from the PEG 300 -1500 which are the PEGs of claim 1.

Tovey mentions PEG but does not specify the molecular weight of the type of PEG that could be used.

Remington provides a general description of tabletting excipients and binders but does not address the specific problems involved when a calcium salt and Vitamin D are formulated into a pharmaceutical composition.

In the development of the claimed product, the applicants were unable to make a usable product using PVP, PEG

6000, mannitol, maltodextrin alone or in combination with croscarmellose Na under wet conditions.

The cited prior art does not make obvious the claimed composition and for these reasons, it is requested that this ground of rejection be withdrawn.

New claim 19 points out a preferred amount of Vitamin D and calcium salt which is disclosed in the Examples of the present application.

An early and favorable action is earnestly solicited.

Respectfully submitted,

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Marked up copy of amended claim:

1. (twice amended) A pharmaceutical composition [containing as] which consists essentially of [active principles] Vitamin D_3 and a calcium salt, as active principles [which comprises] and a binding agent selected from the group consisting of propylene glycol, a polyethylene glycol of molecular weight between 300 and 1500, liquid paraffin and silicone oil, said Vitamin D being present in an amount of 500-1000 I.U. of Vitamin D and said calcium salt being present in a ratio of 1-2 g of calcium, calculated as elemental calcium, for each 500-1000 I.U. of Vitamin D.